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Original Article

The clinical and biochemical features of complicated falciparum malarial nephropathy

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الملخص

أهداف البحث: تهدف هذه الدراسة إلى استكشاف تأثر الكلى من مضاعفات الملاريا المنجلية كما لوحظ على الأطفال المنومين بالمستشفى.

طرق البحث: أجريت هذه الدراسة خلال أربعة أعوام متتالية على الأطفال المصابين باعتلال الكلى نتيجة الملاريا من عمر ٦ أشهر إلى ١٤عاما. وتم التأكد من الملاريا عن طريق الفحص المجهري لمسحة الدم. وتم عمل تقييم سريري مفصل وفحوصات لمعرفة تعدد الأعضاء المتضررة مع التركيز بشكل خاص على تضرر الكلى. كما رصد التدرج لحصول قصور كلوي حاد وفقا لشبكة تدرج القصور الكلوي الحاد المعطى من ثلاث مجموعات من المرضى، التي تم أيضا تعديلها بواسطة التدرج التالي: خطورة, وضرر, وفشل, وفقدان, والمرحلة النهائية لمرض الكلى.

النتائج: من بين ٣٥٠ مصابا بالملاريا, وجد لدى ٥٦ (١٦%) تضرر كلوي. وكانت أعمار ١٤٠ (٤٠%) مصابا ما بين ٥-١٠ أعوام. كما لوحظ ضرر كلوي خطير لدى ١٤ (٢٥%) من الأطفال أعمارهم بين ١٠-١٤ عاما. ووجد قلة/انقطاع البول عند ٤٠ (٤,٧١%) من المصابين، ووذمة عامة عند ٣٣ (٩,٥٨%) من الأطفال من بداية الإصابة بالملاريا. وظهر لدى ٤٧ من الحالات اختلالا في وظائف عدد من الأعضاء, بينما ٩ حالات كان لديها فشل كلوي فقط. كما وجد أن المصابين بالملاريا المسببة لاعتلال الكبد والكلى أكثر عرضة للوفاة من المصابين باعتلال الكلى فقط.

الاستنتاجات: تختلف أطياف اعتلال الكلى بسبب الملاريا عند الأطفال بدرجة كبيرة تتراوح من وجود بروتين بالبول بدون أعراض إلى مراحل متقدمة من القصور الكلوي الحاد. وتأثر الكلى أكثر شيوعا وخطورة في الملاريا المنجلية. الأطفال الذين تتراوح أعمارهم بين ٥-١٤ عاما مع قلة/انقطاع البول, وأعراض آزوتيمية, وتغيرات بالمعادن واعتلال كبدي هم أكثر عرضة لمراحل متقدمة من القصور الكلوي الحاد وبالتالي زيادة خطر الوفاة.

الكلمات المفتاحية: قصور كلوي حاد؛ نقص صوديوم الدم؛ الملاريا المسببة لاعتلال الكلى؛ الملاريا المنجلية.

Abstract

Objective: This study aimed to explore renal involvement in complicated falciparum malaria as observed in hospitalized children.

Methods: This prospective study was conducted for four consecutive years with children 6 months to 14 years old who were affected by malarial nephropathy. Malaria was confirmed by microscopic examination of a blood smear. Detailed clinical evaluation and investigations were carried out to determine multi-organ involvement with special emphasis on renal functions. The staging for Acute Kidney Injury (AKI) was carried out as per Acute Kidney Injury Network Staging, which provided three groups of patients who were further modified by Risk, Injury, Failure, Loss, End stage renal disease (RIFLE) staging.

Results: Out of 350 cases with malaria, 56 (16%) cases had nephropathy. One-hundred-forty cases (40%) were aged between 5 and 10 years. Serious renal involvement was observed in 14 (25%) children who were 10–14 years old. Oligo-anuria was found in 40 (71.4%) cases, and generalized oedema was found in 33 (58.9%) children from the onset of malaria. Approximately 47 cases showed associated multi-organ dysfunction, and 9 cases had isolated renal failure. Malaria-induced hepatopathy and nephropathy had a higher risk of death than nephropathy alone.

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Conclusion: The spectrum of malarial nephropathy in children is highly variable, ranging from asymptomatic proteinuria to advanced stages of AKI. Renal involvement is more common and severe in *P. falciparum*. Children aged between 5 and 14 years and those with oligo-anuria, symptomatic azotaemia, electrolyte abnormalities and hepatopathy are more likely to develop advanced stage AKI and subsequently have an increased risk of mortality.

Keywords: AKI; Children; Hyponatremia; Malarial nephropathy; *Plasmodium falciparum*

Introduction

Malaria remains a serious health problem in many parts of the world. It causes high morbidity and threatens many lives in developing countries each year. Humans are generally infected by four species of malaria parasites.[1] In India, 60−75% of infections are due to *Plasmodium vivax* and 35−40% of infections are due to *Plasmodium falciparum*. Only a few cases of *Plasmodium malariae* have been reported from Orissa and Karnataka, although infections with a fifth parasite, *Plasmodium Knowlesi*, are known to occur in humans on the islands of Borneo and peninsular Malaysia.[2,3] Malarial acute renal failure is commonly found in non-immune adults and older children with falciparum malaria. The occurrence of acute kidney injury (AKI) in severe falciparum malaria is quite common in Southeast Asia and the Indian subcontinent where the intensity of malaria transmission is usually low, with occasional micro-foci of intense transmission.[4] In India, most malaria cases are contributed by the state of Odisha. Although Odisha has a population of 36.7 million (3.5%), it contributes 25% of the total 1.5 to 2 million annual malaria case reports, 39.5% of *P. falciparum* malaria and 30% of deaths due to malaria in India. The five major manifestations of severe falciparum malaria in children are cerebral malaria, severe anaemia and metabolic acidosis, but renal failure is not commonly encountered.[5−7] Although there have been studies describing the association of AKI with malaria in adults, very few have been reported in children.[8] *P. falciparum* is responsible for the most severe, complicated and fatal form of the disease. AKI commonly occurs in *P. falciparum* malaria, although it is rare in *P. vivax* malaria. The incidence in India includes 13% in northeast (NE) India, 17.2% in Orissa and 17.8% in Delhi. Previously, ARF was rare in children but has been increasing in older children. AKI is multifactorial and has a high mortality rate, especially for late referrals or if renal transplant therapy is not available. The resurgence of malaria in Orissa provided us an opportunity to study the changing trends in malarial AKI and its correlation with the parasite species, severity of infection, clinical course and prognostic factors.

Materials and Methods

The present study is prospective, and the incidence of malarial nephropathy along with the clinical features, lab parameters, treatment and outcome were documented. A study of renal involvement in complicated falciparum malaria in hospitalized children was undertaken for 3 years. All children 6 months to 14 years old who were admitted with severe falciparum malaria were subjected to a blood smear examination (thick and thin) for malaria parasites. Smear examination was performed every sixth hour for the first 72 h. Among those admitted, 56 children who met the definition of malarial nephropathy[9,10] were included in this study. A detailed history was taken, and a detailed examination performed with special focus on blood pressure and urine output (<1 ml/kg/h). All patients were investigated for serum urea, creatinine (>1.5 mg/dl) and proteinuria ≥2+ by the dipstick method or abnormal cast in the urine. Hepatopathy was defined as a rise in serum bilirubin along with a rise in serum ALT levels to more than three times the upper limit of normal.

Acute Kidney Injury (AKI) was defined as an increase in serum creatinine (≥0.3 mg/dl) within 48 h or an increase in serum creatinine >1.5 times baseline, which is presumed or known to have occurred with 7 days or UO <0.5 ml/kg/hr for 6 h. AKI Staging was recorded as per Acute Kidney Injury Network (AKIN) staging into 3 groups: Stage I, II and III, which is a modification of the Risk, Injury, Failure, Loss, End (RIFLE) stage renal disease criteria. The RIFLE criteria are based on decreases in estimated creatinine clearance (eccL) and urine output. Risk was defined as an eccL decrease by 25% or urine output <0.5 ml/kg/hr for 8 h. Injury was defined as an eccL decrease by 50% or urine output of <0.5 ml/kg/hr for 16 h. Failure was defined as an eccL decrease by 75% or eccL< 35 ml/min/m2 or urine output <0.5 ml/kg/hr for 24 h or being anuric for 12 h. Loss was defined as persistent ARF, which is complete loss of kidney function for 4 weeks. End stage renal disease was defined as end stage kidney disease for >3 months.

Serum electrolytes, bilirubin and urine analysis were performed. All of the findings, treatment responses and outcomes were recorded. Detailed clinical evaluation and investigations were carried out to detect multi-organ dysfunction with special emphasis on renal involvement. The data were stored and analysed by Microsoft Excel software. Children with severe malaria but who were smear negative, those who died immediately and patients with an ARF other than malaria were excluded from this study. All patients were treated according to the National Vector Borne Disease Control Programme guidelines.[11] Complications were managed according to the existing hospital guidelines. Patients were followed up after 3 months of discharge for the resolution of nephropathy. During follow up, their clinical status and renal function tests were noted.

Results

In this prospective study, 56 (16%) out of 350 malaria patients had renal involvement (Table 1). Out of 56 cases of